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Note from the editor: This article is unusual for several reasons: 1.) It is a monograph--longer than an article but shorter than a book; 2.) *Skeptic* usually features several voices on one subject, but because of the length we decided to allow the AIDS skeptics to respond in the next issue; 3.) Those who do not wish to read the entire article can glean the terms of the debate from certain subtitles and sidebars, especially in Part 1; 4.) Dr. Harris has made an original contribution to the discussion of the AIDS controversy in his analysis of the definition of AIDS, in particular in his use of Venn Diagrams to specify what is unique to AIDS and what is not. *Skeptic* is honored to publish this important contribution to the field and rather than apologize for the length of the article, we remind our readers that the magazine includes its usual array of columns, essays, articles, news items, and forum letters.

THE AIDS HERESIES

A Case Study in Skepticism Taken Too Far

"Felix qui potuit rerum cognoscere causas."--Virgil ("Fortunate is the man who understands the causes of things.")

"It's the virus, stupid." --Dr. David D. Ho, AIDS Researcher

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ABSTRACT

Nobelist Kary Mullis once asked for a reference paper with the simple statement "HIV causes AIDS." This article reviews the modern argument for the HIV/AIDS hypothesis, covering main lines of evidence from human epidemiology and experimental animal virus research. Special attention is paid to the issue of how AIDS may be defined so that the possibility of AIDS without HIV may still be theoretically discussed. Major emphasis throughout this article is placed on the arguments of modern HIV/AIDS skeptics, Peter Duesberg and Robert Root-Bernstein, who do not believe that HIV has a central role in AIDS. It is concluded that HIV/AIDS skeptics have chosen overly broad definitions of AIDS which are not clinically useful, and which would, if employed, result in many confusing diagnoses of "AIDS" and "HIV-free AIDS" in people with good prognoses. HIV is one of a closely-related family of viruses which causes AIDS-like immunodeficiency diseases in a number of animals species, and HIV/AIDS skeptics have ignored or minimized this research in order to construct needlessly complicated alternative hypotheses for the cause of AIDS. These alternative views are based on correlations between AIDS and toxin exposure shown by epidemiologists to be artificial a decade ago, but which skeptics still refuse to abandon. Examination of the HIV/AIDS controversy thus allows us to draw some general lessons about how skepticism in science works, and the ways in which it can go pathologically awry.

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INTRODUCTION: A DIALOGUE IN INDUCTIVE FRUSTRATION

Let us suppose that you have a bright and iconoclastic friend who smokes three packs of cigarettes a day. You remark one day that you would like to see him quit the habit, since he is certainly increasing his chances of lung cancer.

"Prove it," he says.

"Well," you begin, "the Surgeon General and a lot of scientists and doctors say you should quit...."

"Come now!" says your friend, "Since when did you become a fan of The Argument From Authority? I can find you scientists who do NOT believe I necessarily should quit; as well as a lot of intelligent business executives."

"Sure, but all those scientists and executives are paid by tobacco companies or grants from the Tobacco Institute," you protest.

"Well, what do you expect?" says your friend, lighting up and taking a satisfying drag. "Whenever scientists take an anti-establishment position, funding is cut off. The poor scientists then don't have anyone else to support their research but the Tobacco Institute. Do you expect them to drop out of research just because they hold unpopular opinions?"

"Okay, let's look at the data," you say. "What about the fact that 90% of lung cancer occurs in smokers?"

"Yes," says your friend, "and that means that 10% of it occurs in non-smokers, doesn't it? Obviously the 'cigarettes = lung cancer' hypothesis doesn't explain all lung cancer. Even for smokers there must be 'co-factors.' Heck, my grandfather smoked three packs a day right up to the day he was hit by a drunk driver at the age of 92. A lot of people smoke for a whole lifetime and never get cancer."

"Look, I didn't say the correlation was perfect!" you protest. "But it is certainly there. Two-pack-a-day people have 13 times the lung cancer risk of non-smokers."

"Oh, really?" your friend says, "Now, where do you get that number? I suppose somebody did an experiment where they got together a group of nonsmokers and randomized them to start smoking, or else stay smoke-free, and then made sure each and every person did as told for the next 40 years, so as not to bias the results. I must've missed that study."

"You know there is no such study. That experiment would have been impossible, since you can't enforce a random protocol like that. People will start or stop on their own. And besides, any experiment where you try to keep people from quitting would be immoral, since smoking causes cancer."

"So you admit you don't have any study where the two groups of smokers and nonsmokers are exactly equivalent, and only differing by chance or random draw? In every study the smokers and the nonsmokers are self-selected for their behavior and bound to be different not only in smoking behavior, but also because of whatever made them smoke or not smoke to begin with, right?! Not exactly great science, if you ask my layman's opinion."

"But when smokers quit, we know their risk of dying drops," you retort.

"You mean with regard to the smokers who don't quit? So what? The people who quit smoking did so for a reason other than chance or the experimental flip of a coin and again that means they will differ in some way other than their not smoking. Besides, did you know that for the first year after quitting, the risk of death for a new quitter actually goes up with regard to his fellow smokers who keep right on smoking?"

"I knew you'd bring that up. The mortality goes up for the quitter group for a while after they quit only because those people who quit are quite often sick, and that's why they quit."

"If so that makes my point about self-selection, doesn't it? You're saying that in that first year of quitting, the higher death rate of quitters is caused by another factor in our study other than smoking--namely, sickness. Well, so long as we're talking about such third factors, I have a hunch that stress causes cancer, and stressed-out people take up smoking to try to relieve the stress, and that's why there is more cancer in smokers, not because of smoking. Moveover, maybe the act of quitting stresses people out, and that's really why quitters die faster in that first year after quitting. Smoking is just a marker for stress--what you scientists call a "proxy variable."

"All this is ridiculous! You're just using your intellect to make you believe something you want to believe for other reasons. There is experimental evidence! Smoking causes lung cancer in lab animals! Are THEY stressed?"

"Actually, yes--have you seen what they do to them in a modern lab? Ever seen one of those rabbits with a leather muzzle over its nose, and a cigarette stuck in it which it can't take out? But anyway, I don't even believe you can find me a report of an experiment in which smoking causes lung cancer in animals."

Back you go to the scientific literature. And you find nothing. There is no such paper . . . .

Medical Induction

As this fact-based, fictional dialogue demonstrates, because there are many intellectual steps which are not perfectly secure in any generalization, even the most detailed inductive argument only goes so far toward proof. Not only may the same evidence mean different things to different people, it is more difficult to get people to follow a complicated inductive-reasoning trail when they dislike, or are threatened by, the conclusion at the end.

In the medical sciences, assembling an irrefutable argument for causation is sometimes an impossible task for the same reason it is in astronomy or paleontology: the direct and definitive experiment cannot be done. Scientists cannot travel back in time to watch dinosaurs, nor can they influence the behavior of planets or stars. In medicine, a common difficulty is that the necessary human interventive experiments to perfectly assess "risk factors" for harm may be unethical, and so these risks cannot be studied directly by experiment either.1 How, then, do we come to "know" what things cause lung cancer or AIDS? For that matter, how do we come to know with any confidence that tyrannosaurs ate meat, or what generates the sun's energy? In other words: how do we ever infer causation from looking at events (or records of events) which we cannot influence?

However we do it, it does seem that it can (to some extent) be done. Modern science depends on the fact that "correct" causal relationships can often be guessed entirely from logical and indirect observational tests of competing theories, even where direct experimentation is not possible. This is done using help from knowledge of simpler causal mechanisms which we have gained from similar systems in which experimentation

is possible. As Einstein observed, one of the most amazing things about the universe is that this kind of inference is possible at all.

Of course, the overall results of this kind of theorizing, like those of any inductive process, are never certain. Still, whenever inferential theories in science finally do become directly testable by some new experimental technique, they often prove to be surprisingly sound. Why this should be true remains the deep mystery that it was for Einstein.

It is because of an inferential process, based on many lines of evidence, that we can be reasonably confident of the tobacco causation of much of lung cancer, even in the absence of a definitive experimental study. In the same way, an examination of a large body of related facts allows us reasonable confidence about the causation of other diseases-- even a disease far more complicated than lung cancer, and with even more money and passion involved on both sides of the issue.

PART I

THE AIDS SKEPTICS AND THEIR CLAIMS

Should We Be Skeptical?

Recently, several popular lay publications (*Reason*, *Spin*, *New York Native*) have run articles calling into question the theory that the viral agent with the conclusion-asserting name, the "human immunodeficiency virus (HIV)," is the cause of the epidemic of human acquired immune deficiency syndrome, known as AIDS.

What do we mean by talking of the "cause" of AIDS? We know that the common cold or the flu--indeed all infectious diseases--are in some sense "caused" not only by the organism. Also important in the causal chain are host factors (such as immune response), and even simple host-overwhelming factors, such as the infectious dose of organism which enters the body (called the "inoculum"). These additional causal factors, which have nothing to do with the microbe itself, can be extremely important. They may in some cases outweigh everything else. Nevertheless, because the smallpox virus (for example) is necessary for smallpox, medical science still regards it as "causal" in the sense that if there is no microbe, there is no illness. Eliminate the smallpox virus from the population and one eliminates the disease (as was in fact done in the 1970s).

Even this kind of "causal" connection between a disease syndrome and infectious agent is what is under attack in recent articles about HIV and AIDS. Some skeptics have claimed not only that HIV is not the only external factor necessary for AIDS, but that if HIV were eliminated from the Earth, at least some AIDS would still be with us. Still others have gone further and claimed that HIV infection is totally harmless and does not even contribute to the development of AIDS. These people believe that if HIV were to disappear, AIDS would continue exactly as before.

In what follows, we will examine the best evidence behind what most researchers believe is the role of HIV and other factors in AIDS. We will also examine leading skeptical views on the causation of AIDS. Because a great deal of published research is available on this issue, our examination of AIDS will also let us illustrate how science closes in on cause and effect, even when direct experimental "proof" is not available.

We will thus be interested in not only AIDS, but also larger questions about science, and scientific debate. What makes a good scientific theory, and what makes a poor one? Are there reasons for hope in looking at the disease of AIDS in particular, and the workings of the biomedical scientific "establishment" in general? Are we making any progress with AIDS, or just wasting billions each year chasing fantasies?

This essay will argue that we are not wasting all that money, and that when it comes to critics of the HIV/AIDS hypothesis, we have a practical case in which skepticism has been taken too far. Science, we are happy to report, still works, and it is making progress with AIDS. That some critics have failed to recognize this only highlights the fact that science is only partly an empirical enterprise, and that it also has an intuitive and aesthetic side which is subject to arguments over taste. This is not a thing which is taught to students in schools, but it is a concept key to understanding most scientific controversies.

Defining AIDS

Scientific problem-solving begins with definitions, and in choosing a definition for AIDS we run immediately into the HIV/AIDS controversy. Some of the difficulty is that definitions, even in science, are chosen partly on aesthetic grounds, partly on utilitarian ones.

In medical science we rarely know in detail at the molecular or even cellular level what causes most human illness, and so in our ignorance we are often forced to work with "disease syndromes," which are collections of symptoms and sometimes lab tests which seem to "go together." In order to usefully define a "disease syndrome" we need to pick our defining characteristics so as to include all of the sick people who we are interested in for good clinical reasons, and exclude everyone else.

What are good clinical reasons? In medicine there is not much point in defining a new "disease" which, when present, makes no difference in either prognosis or treatment. Nor is there any point in defining a disease so poorly that it fails to capture all the sick people who seem to have pretty much the same thing wrong with them from the prognosis or treatment viewpoint. If (as always happens) we lack information about what impact certain definitional characteristics have upon treatment or prognosis, then we are forced to guess, as best we can, what definition will be most useful. It is at this point, in deciding whether two people have "pretty much" the same thing wrong with them, that aesthetic and intuitive considerations unavoidably enter into medical science.

Utility imposes other constraints, too. A disease definition which is to be used during a hunt for the disease's causation, should not assume any cause which is in question. In other words, if we choose a definition for AIDS which requires infection with the HIV virus (the current way it is done in many countries, including the U.S.), then we will have chosen our terms so as to be of little help in the question of whether HIV causes AIDS. Obviously, it would be nothing remarkable if we "discovered" that 100% of people with AIDS were infected with HIV, if we defined AIDS in such a way as to require HIV infection.

In re-opening the question of the cause of AIDS, what we need is a modified AIDS definition which does not involve HIV, so that the question of whether or not all AIDS cases are infected with HIV is an empiric one, not simply a semantic one. When we have a suitable HIV-free candidate definition for AIDS, we can then ask two critical questions about it: 1) Have we captured with our definition all of the people with the new medical problem that we historically came up with the AIDS label, in order to describe and encompass in the first place? 2) If we test our defined group, are 100% of the people encompassed by our AIDS definition found to be infected with HIV, an otherwise rare virus in the population? If the answer to both these questions is yes, then HIV is promoted to a good candidate for a cause of AIDS. If either answer is no, then the HIV/AIDS hypothesis obviously has severe problems right from the start.

Fortunately, however, we can easily construct a workable definition of AIDS which does not include any reference to HIV, but which still describes the new epidemic in which we are interested. Such a definition will not be the standard one, of course, but since the standard modern HIV-containing AIDS definition is unusable for this purpose, both we and the AIDS skeptics are required to construct special AIDS definitions even to continue to talk about the problem of causation.

Redefining AIDS:
Acquired Immune Failure Syndrome

What is the best way to define AIDS without reference to HIV? Acquired Immune Deficiency Syndrome is the name historically chosen for a new medical syndrome which is essentially 100% fatal, and thus in defining it we are looking for people with an immune deficiency in the range which is life-threatening and will continue to grow relentlessly worse until life is impossible.

One possible way to define immune deficiency would be to define it by what problems it causes--for instance, one could pick people who have gotten so-called "opportunistic infections" or strange infections which are seldom if ever seen in people whose immune systems are fully functional. In the early days of AIDS, before HIV was discovered, the syndrome was indeed defined using such opportunistic diseases (Fig. la), and people with these infections are still included in the federal Centers for Disease Control (C.D.C.) clinical surveillance definition of AIDS (but now only if they are also HIV infected). We will not be able to use this C.D.C. definition (Fig. lc). Not only does it assume HIV

infection, but for historical, political, and technical reasons, it also is constructed in a way which does not assess current immune status in the best way.

Why is this? The basic problem is that only a limited amount of information about a person's immune system function flows from the bare fact that they have an "opportunistic" infection. Certainly there is a good correlation between immune function and what kind of opportunistic infections occur, but the correlation is far from perfect, since opportunistic infection risk is influenced by not only immune status, but also by the quality of what we may term the infectious "assault" to the system. The assault in turn is influenced by a person's physical location, infection contacts, personal habits, and other exposure factors both known and unknown. In the end, assault differences insure that some unlucky, highly infection-exposed people manage to contract opportunistic infections when only mildly immune compromised (though these are rarely fatal). By contrast, the same assault differences insure that other people who are badly immunologically impaired may escape opportunistic infections for an amazingly long time, simply by missing the microbes which will kill them (Fig. 1a).

When it comes to immune function, then, it is better to have a direct test which is not subject to uncontrolled variables such as which microbes happen to be in the air or drinking water, and how many. Such a test exists. Quite early in the history of AIDS, it was found that the immune defect in this disease is peculiar, and that it most visibly involves a particular kind of cell in blood and lymphatic tissues (lymph "nodes"), called "T-lymphocytes." In the syndrome of AIDS, certain T-lymphocytes gradually disappear from both blood and lymph tissues, and a simple T-lymphocyte count in the blood can tell how serious the reduction has been in both places (since blood lymphocytes come from the lymphatics). The arm of the immune system which is controlled most directly by T-lymphocytes (the body's defense against viruses and fungi) is what is most defective in AIDS, and viral and fungal infections are the main opportunistic infections which appear and cause death in AIDS.

AIDS is so specific in its attack that scientists eventually found that only one subset of T-lymphocytes was initially hardest-hit. This was the so-called CD4+ or "helper" T-lymphocyte, which has the job of stimulating the immune system. The other major type of blood T-lymphocyte, the CD8+ or "suppressor" lymphocyte, is involved in shutting the immune system down; in AIDS, CD8+ lymphocyte blood numbers increase early in the disease, and are not decreased until near the very end of the disease process, when they may also disappear.

CD4+ lymphocyte blood counts tell much of the story in AIDS and other immunodeficiencies involving the T-lymphocyte immune system. A healthy adult might have a CD4+ lymphocyte count of 800 to 1000, with a CD8+ count half of this. These are normal values. Under physical stress, injury, or chronic infection, CD4+ lymphocyte count might drop to 500 (to even less than the CD8+ count), and mild, non-fatal opportunistic infections might be the result. A CD4+ count less than the CD8+ count was once used as a crude marker for AIDS, but today with progress we know that this

immune state is non- specific. In AIDS, things eventually become much worse than this, and the worse things get, the fewer possible alternative causes are possible.

In full-blown AIDS, as defined by opportunistic infections and other problems, the CD4+ count is usually below 200. It is at such count levels that Kaposi's sarcoma (a tumor perhaps caused by a virus) and life-threatening infections begin to appear, although approximately 95% of AIDS patients survive beyond this level of decline.2 Another feature of AIDS, however, is that inevitably the count grows worse over time. Today, in the modern era of antibiotics and more knowledgeable care, 85% of AIDS patients live to see their CD4+ lymphocyte count drop below 50.3 Famous AIDS sufferer Kimberly Bergalis, for instance, had her CD4+ count drop to 41 before her disease was even diagnosed.4 Many AIDS patients today go all the way to CD4+ counts of zero before the inevitable final infection or other complication. It is because of the implacable and more or less irreversible loss of vital T-cells that AIDS remains a fatal condition, with an average time span of less than two years between the first opportunistic infection and death.

If we wish to define AIDS in terms of immune failure, the essential question is where do we draw the line, so as to include almost all people with the new immunodeficiency epidemic, who are going to die from it, but exclude everyone else? If we simply define "immune deficiency" as a sustained CD4+ lymphocyte count of less than 200 (where death begins to become more likely), we will capture about 95% of people who die of what the C.D.C. now defines as "AIDS" (Fig. lb).

Previous to the epidemic of AIDS, of course, people did die of immune failure with low T-lymphocyte counts (including low CD4+ counts) for other reasons, and they continue to do so now. Thus, we must also exclude from our AIDS definition all those people who have one of the classic reasons for a very low T-lymphocyte count--reasons which were well-known before the AIDS era (cancer, malnutrition, tuberculosis, radiation, chemotherapy, etc). These people do not have AIDS, because the historical epidemic of AIDS consisted of people with no T-lymphocytes, and yet no known reason for it. These people had appeared newly on the scene in the 1980's with evidence of a fatal kind of immune failure which was acquired, meaning that it was an epidemic problem of something "picked up" by previously healthy people.

So let us simply collect all the people we can find with CD4+ counts remaining below 200 (for a few months) without known reason, and test them for HIV. When we do, we find that essentially all are HIV infected, and any who are not do not look at all like typical AIDS patients (as we will see). This, despite the fact that only 0.3% of the general population carries this virus. Thus, at this point we have no evidence yet to directly contradict the simple theory that HIV causes 100% of our conservatively defined "AIDS." AIDS skeptics will need different definitions in order to find HIV-free AIDS. (Fig. 1d and 1e).

Enter the AIDS Skeptics

The view that HIV plays no role in AIDS has been most notably put forth by Peter H. Duesberg, professor of molecular and cell biology at the University of California at Berkeley. A German emigree, he was originally trained in chemistry. On arriving in the U.S. in 1964 he began work in the field of viral molecular biology at Berkeley, where in 1970 he co- discovered the genetic basis for the carcinogenic action of the Rous sarcoma retrovirus. In 1987 he began publicly questioning the role of HIV in AIDS, a stand which has made him the center of the present HIV/AIDS controversy. Duesberg's most recent book is called Why We Will Never Win the War on AIDS (1994), co-authored by a Berkeley graduate student and one-time protege Bryan J. Ellison. The book has been plagued by trouble. According to a message issued October 13, 1994 by the Group for the Scientific Reappraisal of the HIV/AIDS Hypothesis, this manuscript was published unilaterally by Ellison without Duesberg's consent, following failed editorial negotiations with the original contracting publisher (St. Martin's Press). According to Duesberg, the editor had asked for additional documentation, clarification, and elimination of material which might be considered unfair to individuals. Duesberg was willing to cooperate but Ellison was not. Following Ellison's publication of the manuscript at Inside Story Communications (a newsletter edited by Ellison), Duesberg severed relations with Ellison and is seeking an injunction against further publication of the book. The cooperation of James Tabulse, publisher of the Group's newsletter Rethinking AIDS, with Ellison, has meant that the Duesberg's Group has decided to severe relations with this publication as well. They now publish a new newsletter called Reappraising AIDS. Since Duesberg has questioned only publication and editorial rights for the new book and has not repudiated any of its contents, the book is used in this essay (see page references) as a source of Duesberg's views. A major Duesberg essay is also used.5

At the other end of the skeptic spectrum are hybrid arguments raised by Robert Root-Bernstein, an associate professor of physiology, winner of a MacArthur "genius" award, and author of Rethinking AIDS6, the most carefully- documented work to yet assail the prevailing medical views on HIV and AIDS (see page references). Root-Bernstein is less radical than Duesberg, arguing for a somewhat less central role for HIV in AIDS than is generally given it, but still allowing for the virus to have some part in the etiology of the disease.

Since Duesberg's original challenge, which has been the cause of much formal debate in the literature7, a number of scientists, physicians, and lay persons have taken up the cause for a "re-appraisal" of the idea that HIV is the major causal factor, or even one of the major causal factors, in AIDS. Most respectable is the Group for the Scientific Reappraisal of the HIV/AIDS Hypothesis, which has collected over 200 signatures of physicians and scientists, including those of Nobelists Walter Gilbert and Kary Mullis. This group has campaigned to remove the requirement for HIV infection from any medical definition of AIDS, feeling that using this criterion is at best premature, and prejudices any hunt for alternative explanations for the disease.

Almost all critics of the AIDS/HIV hypothesis have one thing in common: they insist on using a much broader definition of AIDS than we have proposed, a definition which

virtually guarantees that some people who fit the critics' AIDS definition will not be HIV infected.

To be fair, there is some historical precedent for using a definition of AIDS which relies solely on the patient developing one of a certain list of the most serious and specific opportunistic infections, since this was the way the disease was diagnosed before HIV testing became available in 1985 (compare Fig. 1a and ld). Today we know that almost all such people with pre-1985 defined "AIDS" are infected with HIV--indeed this was known in late 1983, before the official announcement of viral cause was made the following year. But today we know this figure would not quite be 100%.13 As we will see below, there is evidence that the few HIV-negatives in this group will be people with lesser degrees of immune suppression (higher CD4+ counts), who will not progress to worse immune function, or quickly die. (Fig. 1c). It seems reasonable, then, with what we know today, to simply exclude them--since we know that this is not the characteristic picture of AIDS. Again, it is most reasonable for our purposes to diagnose AIDS on the basis of immune function (CD4+ levels) only, since it is immune function, not infection status, which correlates with short-term prognosis in CD4+ immunosuppressed people.

The skeptics, however, will have none of this, and in their definitions are seemingly less interested in clinical utility than they are in collecting ammunition for an argument. The more broadly AIDS is defined, the more "HIV- free AIDS" cases skeptics can assemble, and these, in turn, can be used as evidence to the lay public that HIV cannot be the cause of AIDS.

Duesberg, for instance,5 has insisted upon retaining the early 1980's observation that a CD4+/CD8+ lymphocyte count ratio of less than 1.0 is often seen in AIDS, and he has decided that such a ratio, even in the absence of opportunistic infection, is synonymous with AIDS (p. 260). Duesberg now calls this ratio an "AIDS-defining immunodeficiency," and counts people with this lab result as part of "HIV-negative AIDS," in his shocking and too-often repeated statistic that there are "3,000 documented HIV-free AIDS cases."8 Here again, Duesberg's chosen definition of AIDS is less than useful because people with such mild immunosuppression as he uses to define "AIDS" are not the people who are dying, or are shortly destined to die. AIDS is nothing if not a fatal epidemic, and insisting that mildly compromised persons who may or may not eventually get any worse be labeled as having "AIDS," as Duesberg routinely does, only serves to confuse the issue (Fig le).

There is a general trend for AIDS skeptics to overdramatize levels of immune deficiency which are not clinically very significant. For example, Root-Bernstein (p. 262), in characterizing a study of HIV-negative men newly infected with CMV virus, notes that for a time, some of the men had CD4+/CD8+ cell ratios of less than 0.4, a figure which he claims "represents extreme immune suppression." During viral infections such CD4+ depressions are transient. In AIDS, however, this ratio would typically be far less than 0.3, and thus these men would not be mistaken for the current C.D.C. immunological definition of AIDS, even if they were HIV-positive.9 The level of immunosuppression associated with a ratio of only 0.4 is not associated with significant risk of death by

opportunistic infection. You might wonder how we are justified in calling a ratio of 0.4 "extreme immune suppression," if people rarely die from it, as they are known to do in AIDS. Root-Bernstein does not say--indeed, does not even raise the issue. The AIDS skeptics' overdrawn interpretation of the clinical significance of lab results is one of the places in which absence of medical training shows most clearly.

Indeed, Duesberg's paper5 and Root-Bernstein's book6 each contain descriptions of groups of HIV-free people who are somewhat immunosuppressed due to low CD4+ counts, or low CD4+/CD8+ ratios, but not severely so, as defined by our straightforward criteria of having a significant risk of infectious death due to T-lymphocyte loss. These immune deficient patients in the AIDS skeptics' literature are presented along with the inference that perhaps somewhere there exist people with these immune suppressive factors, or combinations of them, who are severely T-lymphocyte immunosuppressed for long periods of time (as AIDS patients are), and yet still without having HIV. Duesberg and Root- Bernstein only have one difficulty in this argument--neither has been able to actually find any such people.

HIV-Free AIDS?

Hypotheses may be disproved by the right data with relative ease, and cases of HIV-free AIDS would disprove the idea that HIV causes AIDS, in proportion to how often these are found (i.e., if 10% of AIDS cases were HIV-free, this would prove that HIV is not the cause of at least 10% of AIDS). Thus, Duesberg and Root-Bernstein are not the only ones who have been looking for HIV-free people who are badly CD4+ lymphocyte immunosuppressed without reason (i.e., good candidates for HIV-free AIDS). Very recently the C.D.C. reported that after a massive search it had only been able to find less than 100 people without HIV infection across the country whose CD4+ counts were at one time less than 300 (not quite in the AIDS-class immunosuppression range of 200, but drawing close). This syndrome was named "ICL" (idiopathic CD4+ lymphocytopenia), meaning "people with low CD4+ lymphocyte counts without a medically-defined disease."

Why was ICL not simply called "HIV-free AIDS?" Critics have darkly suggested that the reason is politics, but in fact there were problems with considering these people as AIDS cases which had nothing to do with AIDS politics or the HIV theory. One difficulty was that people labeled as having "ICL" were found not to come from the AIDS risk groups. They did not use illicit drugs, had not been exposed to blood products, and had no evidence of sexual behavior which would have exposed them to a special infection risk. Thus, as we will see, the most popular alternative AIDS hypotheses did not explain these people either--a fact which did not keep them from being mentioned in nearly every skeptical treatment of the HIV/AIDS issue. What the skeptics had forgotten (or hoped their readers would not notice) was that the immune deficiency of people with ICL did not seem to be acquired.10 What justification was there, then, for calling it AIDS?

Moreover, people with ICL were not only epidemiologically, but often immunologically distinguishable from AIDS cases: their CD4+ lymphocyte counts swung widely, and

transiently, in response to infections, and were often much higher than 300 (in contrast to people with AIDS, whose CD4+ lymphocyte counts tend to stay low and heading on an ever-downward trend). ICL people also often had low total lymphocytes or low CD8+ lymphocyte counts, again indicating that their immune failure did not make much distinction between CD4+ and CD8+ lymphocytes, as classic AIDS does. Clearly, these people did not belong to the classic AIDS groups which began suffering with epidemic immune problems about 1980. They are not part of the new phenomenon of AIDS, and although sometimes suffering from opportunistic infections, did not even seem to share the implacable death rate of AIDS.10

Searches for HIV-negative people who have AIDS-type severe immune suppression have also been taken specifically within AIDS risk groups. Vermund reported in the United States Multicenter Cohort Study that of the 2,713 persistently HIV- negative homosexual men in the study, who had had a total of 22,643 blood tests, only one significantly immunosuppressed man (CD4+ lymphocyte counts persistently less than 300) was found. This man was taking chemotherapy and radiation for cancer, and thus had a very good reason other than his lifestyle to explain his lab results.11 If this study is indicative, then most, if not all, male homosexuals with sustained AIDS-range immune failure are HIV-positive, since it has proved very difficult to find any who are HIV- negative.

Much the same seems to be true in IV drug users: in a study of 1,246 HIV-negative injecting drug users in New York City from 1984 to 1992, for example, only four were found with CD4+ lymphocyte counts less than 300 (if IV drug use per se was a major cause of AIDS, the number should have been far higher). In this small group of four people, even though infected with multiple non-HIV viruses, and with a history of heavy drug use, immune function was stable and without the steady decline in CD4+ lymphocyte counts over a time span of years which is characteristic of all unselected HIV-positive cohorts.12 Thus, in this study also, the few HIV-negative people who could be found with even near-AIDS range immunodepression, were still not behaving medically like people with AIDS.

So far as we know, then, in the United States all people who are a part of this new phenomenon of sustained very low (and declining) CD4+ cell counts in high risk groups, have been infected with HIV. This does not prove that HIV causes AIDS, but it is surely an important clue.

Why Not AIDS Without HIV?

A persistent suggestion by skeptics is that it would be proper to use as an AIDS definition the current C.D.C. definition (which includes all HIV-infected people who have a much expanded list of infections and other problems), but with the HIV criteria removed. (Fig. 1d.) The problem with this suggestion is that definitions of diseases are chosen by the C.D.C. for maximum clinical utility, and HIV criteria in the C.D.C. AIDS definition was not put there only to insure that there would be no HIV-free AIDS. Rather, HIV infection in a person with opportunistic infection is known to be (alone among all other viral infections) a very good predictor of whether immune status will continue to decay until

the person eventually succumbs to opportunistic infections. In people with mildly compromised immune systems, the prognostic importance of an HIV infection (which even critics admit, without admitting causation) is large. Thus, we cannot simply remove HIV status from the C.D.C. definition and still have the definition do what it was designed to do, which is predict impending death by immune failure.

AIDS skeptics know that if "AIDS" is defined only in terms of today's much broader list of "AIDS-defining" diseases and infections (which are meant to be used only in conjunction with HIV status), it is sure to be quite true that the definition will be far too broad to be prognostic. Such opportunistic infections, as critics well know, sometimes happen in the population occasionally even without the most severe CD4+ immunosuppression which is characteristic of people who die with AIDS.

A study by Salvato illustrates this point.13 In the study, medical records over six years for 1500 HIV-positive patients were compared with records for 1,000 HIV-negative patients who had Chronic Fatigue Immunodeficiency Syndrome (CFIDS) and evidence of immune suppression. It was found that the CFIDS patients had fatigue, lymphadenopathy (swollen lymph "nodes") and low grade fevers--but that over the course of six years their problems were not severe. Only one of them developed CD4+ lymphocyte counts less than 300 ("ICL"). Still, two had yeast esophagus infections, a severe opportunistic infection rarely seen other than in AIDS and other people severely immunosuppressed. Three had active CMV virus disease of various tissues--another disease very often seen in AIDS. A total of 486 patients had evidence of yeast infection of the mouth on exam, a condition suggestive of mild immune problems but one not limited to AIDS. The average CD4+ lymphocyte count in these patients (not including the single ICL patient) ranged from 500-1400, with an average of 650. This was significantly lower than normal, but much higher than typical for AIDS.

In this study, 95% of the HIV-negative patients had previously been infected with the EBV, CMV or HHV-6 viruses, and 48% had evidence for continued viral infection (skeptics such as Root-Bernstein have suggested that these viruses have roles in AIDS at least as important as that of HIV, but this study provides evidence against this idea). Most interestingly, these immunocompromised HIV-negative patients were followed from two to six years, and none experienced progressive CD4+ lymphocyte decline (except for the one patient with ICL, who, with treatment of CMV infection, showed increased CD4+ lymphocyte counts again). Such CD4+ count stability is never seen in any random group of HIV- positive people, where average CD4+ count decline with time would be inevitable. The authors conclude: Even after a methodical search in a practice that sees a large number of patients with immune problems, only 1 patient was found to have ICL. However, this study demonstrates that patients with normal CD4 counts can develop AIDS defining opportunistic infections . . . Upon long-term follow-up these patients do not appear to experience progressive CD4 depletion.

Most importantly, no HIV-negative person died in the study, which illustrates the extent to which chronically virally infected, immune-suppressed people can approach the

clinical picture of AIDS (see dark area Fig. 1d), without crossing into the permanent and deadly immune failure which is characteristic only of people with HIV infection.

The reader who is a bit confused at this point should keep in mind simply that the most important thing about the syndrome of AIDS is that it inevitably and rapidly destroys the immune system and kills people. Thus, mild CD4+ depression and opportunistic infections are not always AIDS, for only some of these people (as it turns out, the HIV+ ones) will progress to immune failure. It is immune failure (almost complete sustained CD4+ lymphocyte loss) and death by opportunistic infection which is characteristic of AIDS; and it is only these people who are always HIV infected.

Did the Government Create AIDS?

At the African-American Summit speech in New Orleans in 1989, Louis Farrakhan told his audience: "The spread of international AIDS was an attempt by the U.S. government to decimate the population of central Africa." Last year he told Barbara Walters on ABC's 20/20: "Do you know where the AIDS virus was developed? Right outside of Washington. It is my feeling that the U.S. government is deliberately spreading AIDS." Such paranoid and conspiratorial thinking is not uncommon in history whenever a new and devestating plague destroys a community, as when the Jews were blamed for the Black Death in the 14th century. But this is not the form of AIDS skepticism which I am addressing in this essay, and needless to say there is not a shred of evidence for such an outrageous claim.17

But what if AIDS and immune failure are not really new-- perhaps we just look harder for them now that we recognize them? Could our new theories be warping our views so completely that by now that we have made a new "plague" out of something that was here all the time? Epidemiologically, what can we fairly say about the period before 1980, keeping this possible bias in mind?

With the new ability to test old preserved tissue specimens for HIV, the first thing that becomes apparent is that AIDS is indeed older than 1981--perhaps far older. Deaths from what has since been recognized as HIV infection with immune failure have been seen clinically, without being understood, for at least 35 years, and probably much longer. An HIV-infected British sailor, who had traveled widely, is known to have died with severe immune deficiency and HIV infection in 1959, the earliest proven case of modern AIDS. The diagnosis was made by means of preserved autopsy tissue specimen HIV testing, 30 years after the fact.17

This man's death alone provides good evidence that HIV is not a product of deliberate (government or otherwise) genetic engineering, for in 1959 biologic science was simply too unsophisticated to work with lymphotropic (lymphocyte- infecting) retroviruses like HIV, let alone engineer them.103 If it is anything at all, HIV is an accidental infection of humans with an African primate virus. The genetic material of the most common HIV-1 strain is most similar to that of a virus known to naturally infect chimpanzees, and it may be that HIV's ancestors have been present in Africa, perhaps even in humans, for a very

long time--perhaps thousands of years.18,121 In West Africa, a close cousin of the U.S. HIV-1 strain, called HIV-2, is almost identical to several indigenous African monkey viruses, and almost certainly has been derived from them quite recently in virus evolutionary time (less than several centuries).

The Origins of AIDS

The story of the detective hunt for the cause of AIDS is told with wit and clarity by Randy Shilts in the best-selling book *And the Band Played On*. (In 1994, Shilts, at the age of 42, became a casualty of the disease himself.) Other good histories of the early AIDS epidemic are also available.14

In the U.S., the first AIDS or AIDS-like death that we know for sure was also associated with HIV infection was that of a 17 year-old possibly homosexual male, who died of strange opportunistic infections in 1968, and whose preserved tissues also proved to be harboring HIV genetic material on testing decades later.19 This early AIDS-sufferer had never been out of the country, showing that the virus was already active in the Western Hemisphere in 1968. In corroboration, a 4% fraction of preserved serum samples from IV drug users in this era (1971-2) in the U.S. have been found to be HIV- positive. Apparently HIV viral infection has been present in small contingents of both drug users and homosexual men for some time in the United States.20

Why, then, was the U.S. first hit with an AIDS epidemic only in the 1980s, with HIV infection quickly rising to 50% in some risk-groups? The answer may be that it was not the simple presence of HIV virus in the United States that changed; rather it was the social milieu.

In the late 1960s drug use became far more widespread in the U.S., and the invention of the disposable plastic injection syringe about 1970 made IV drug abuse possible for the first time on a large scale. Also beginning around 1969 (the date of the New York City "Stonewall" riots), homosexuals in the U.S. began to take open political power, and concomitantly one faction of male homosexuals began to engage in the high-infection risk "bathhouse lifestyle" chronicled by Shilts. In addition, the American homosexual-male community was apparently many times re-infected by many world-traveling disease "vectors" from other countries in the 1970s, including an airline steward named Dugas (described in Shilts as the C.D.C. "patient zero") who traveled widely in Europe, Canada, and the U.S., died of AIDS, and is known to have had sex with no less than 40 of the first 248 Americans to be diagnosed with AIDS by April, 1982.14

What happened in the late 1970s in the U.S. is that when a large enough fraction of the American homosexual-male population became infected with HIV, the U.S. blood supply, maintained with volunteer donations only, finally became contaminated with the virus. (This started in 1978, as we know from later testing of archived serum samples taken from homosexual men originally for hepatitis B studies). Similar archived samples tell us that in 1978 the U.S. plasma supply used to make clotting factor for hemophilia treatment became HIV contaminated, no doubt primarily by IV drug users selling plasma

to support a drug habit. The dates are not coincidental--crossover between initial HIV infected groups occurred as some homosexual men experimented with IV drugs in the late 1970s, and male IV drug users in large cities turned to homosexual prostitution in order to obtain drugs. The resulting new epidemic of transfusion and hemophilia-associated AIDS, beginning in 1982 and rising sharply in 1984, helped to bring the acquired nature of AIDS into focus.

The small incidence of AIDS in the American homosexual- male and IV drug-user communities before the late 1970s in no way subtracts from the reality of the dramatic increase in AIDS which took place in the early 1980s on the heels of exploding HIV infection rates in these groups. Although relatively mild immune suppression has apparently always been widespread in many AIDS risk groups, the more complete and devastating immune failure characteristic of AIDS itself has been sporadic and rare in young cancer-free people in any of these groups, until the 1980s.

It is, to be sure, difficult to retrospectively evaluate the health of male homosexuals before the first prospective studies of gay men's health were done in the 1980's AIDS era, but we can be reasonably sure that an epidemic of deadly immune failure among young American men before 1980 would have been duly noted by epidemiologists. AIDS skeptic Root- Bernstein documents a few cases of unexplained opportunistic infection deaths from the medical literature before 1980, but clearly an epidemic of immunosuppressive deaths cannot be seen in the historical record before 1980 by any act of imagination.

By contrast, at present AIDS shows a high and rapidly rising incidence among young men and women in the U.S., and these deaths cannot be simply a new label for an old problem. The reason is that total mortality and cumulated years of life lost to premature death in young persons are observed to be rising rapidly, with all of the change due to AIDS deaths, at the same time other leading categories of mortality remain stable. If mere re-labeling of deaths into different categories was a problem, these "newly recognized" AIDS deaths would come out of other previously defined mortality categories, and this clearly is not happening.21 AIDS, the disease, may be old; but AIDS, the epidemic, is indeed something new.

People with hemophilia, unlike homosexual men, represent a well-defined group with long-term documentable changes in morbidity and mortality, since they had been well-studied as a group before the era of AIDS. This research shows that people with hemophilia began to die of dramatically different things, starting about 1982 (Fig 2).22 A recent check shows little evidence of a special incidence of opportunistic diseases in people with hemophilia in the U.S. from the turn of the century up to 1979, although a low incidence of AIDS could not be ruled out in this study, mostly because some cases of fatal pneumonia had no identified infecting organism,23 and because people with hemophilia as a group are immunosuppressed enough to be somewhat more susceptible than normal to bacterial infections. Significantly, however, in the years before AIDS, people with hemophilia had never been noted to be particularly susceptible to the more obvious fungal infections, such as candida esophagitis, common to AIDS patients and

others with low-lymphocyte type immune deficiency. After 1984, however, this type of AIDS-associated opportunistic infection and immune failure rapidly became the single most common cause of death in people with hemophilia in the U.S.24

The rise in total mortality risk in people with hemophilia was sudden: total mortality in this population, which had been stable in 1982 and 1983, suddenly increased by a factor of approximately 900% in the first quarter of 1984.25 Such an increase in raw numbers of deaths was consistent with an epidemic, or some new very toxic contamination of the clotting factor supply. It is not consistent with slower social changes, slower toxin or immune suppression models, multifactorial causation models, or the idea that people with hemophilia were actually at no greater risk than before (i.e., that again perhaps there had been some kind of "cause of death" re-labeling in response to AIDS hysteria). (Fig. 2.) Mortality figures in hemophilia patients also showed something else important, which was that the new deaths of the late 1980s, by virtue of all being judged "AIDS," demonstrated that most or all of them occurred in people with hemophilia who were HIV-positive. Since these deaths accounted more or less for the entire new increase in mortality, it could be inferred that the mortality rate for HIV-negative people with hemophilia did not increase much in the 1980s, if at all.

How significant was the increase in death rate for HIV- positives in this group? In one Journal of the American Medical Association study it was found that in a cohort of 111 people with hemophilia infected with HIV in the early 1980s, one third had died by 1992.26 Imagine any group of this age (a high school class, perhaps) and imagine an overall 33% mortality rate in less than 10 years. Of the estimated 10,000 people with hemophilia to have been infected with HIV in the early 1980s in the United States, a quarter had been reported to the C.D.C. to have died of AIDS by July of 1993.

Such death rates were especially shocking in view of strides in hemophilia treatment which had been made in the years before. Total life expectancy in people with hemophilia had risen as clotting factor treatment became available through the 1970s, until by 1980 it was nearly normal.23 After 1984, however, life expectancy in this group began a steep decline, and by the early 1990s was at a lower level than at any time since before World War II.24 In the 1980s, total mortality for hemophilia increased in all age groups above nine years of age, and age at death shifted markedly to lower ages, decreasing from 57 years of age in 1979-1981 to 40 years of age in 1987-1989.27 (Fig. 2.)

About 50% of people with hemophilia in the U.S. had been HIV infected by early 1986, when screening and treatment of the clotting factor concentrate stopped HIV spread.28 Still, the long latency of the virus (as long as 15 years for 50% progression to AIDS in this group) caused death rates to rise for long after the window of new HIV infection closed.

The fact that there was a massive and silent HIV infection of half of the people with hemophilia in the early 1980s is beyond question, even for skeptics. The AIDS skeptics' quest to divorce this event from the epidemic of deaths by AIDS in this same group over

the next decade has resulted in some remarkable and curious statements about hemophilia mortality. Duesberg, for instance (p. 216) quotes only older statistics for hemophilia patients from the pre-1986 period, before AIDS deaths became very large. His practice of using randomly reported AIDS and mortality data for people with this disease (which is often notoriously unreliable in the best of circumstances29), instead of the much more reliable cohort study data, also results in figures which minimize the impact of AIDS. Cohort data shows mortality in hemophilia patients to be far higher than Duesberg acknowledges.30

Duesberg has not been alone in ignoring major trends in hemophilia mortality in the last decade. The very misleading statement that people with hemophilia are living "longer than ever" today is one of the standards among the HIV/AIDS skeptic community. Root-Bernstein does no better than Duesberg at providing updated information in this area, offering one paper's 1979 pre-AIDS statistics,23 without update and without qualification, to represent contemporary life expectancy in people with hemophilia in 1993 (p. 247). This represents very sloppy scholarship (something which stands out particularly in Root-Bernstein), but the oversight does allow the author to skip discussion of the pronounced and otherwise awkward peak in life expectancy for hemophilia in the middle 1980s.

Duesberg, though he seems to believe that people with hemophilia have suffered no mortality increases in the age of AIDS, does suggest that people with hemophilia live longer than ever due to recent factor concentrate development, and thus live long enough to die of immunosuppression caused by longer treatments with clotting factor concentrate, instead of from hemophilia (p. 220). Although clotting factor does indeed appear to be mildly immunosuppressive (albeit in a different way than AIDS--CD4+ lymphocyte counts are not affected), the main problem with the hypothesis that clotting factor itself causes AIDS is that two studies of HIV-positive people with hemophilia have found that HIV infection, and not clotting factor use, is the critical risk for AIDS. These studies found that once a person is HIV-positive, risk of AIDS is not related to amount of clotting factor used or severity or type of hemophilia--effects that would have been expected if clotting factor carried a significant immune risk independent of its HIV content.31 Available statistics thus strongly suggest that the known association of clotting factor use and AIDS risk is merely due to the increased risk of being infected with HIV the more clotting factor has been consumed; once HIV infection has occurred, it does not matter how much clotting factor is used.109

AIDS in the 80s

Historically, what happened in the U.S. in 1981 was that in increasing numbers homosexual men began coming to physicians with very, very low CD4+ lymphocyte blood counts (but not lowered counts for other subtypes of lymphocytes), a destroyed immune system with lymphatic tissue destruction, opportunistic infections, and Kaposi's sarcoma. No one who had treated diseases in the male homosexual community could remember having seen anything remotely like what had began happening on an increasingly large scale in the early 1980s.

The year 1981 was not (in retrospect) exactly when the problem started, but rather when the problem first grew large enough in the U.S. to be brought to the attention of the federally-run Centers for Disease Control in Atlanta. It was in the Summer of 1981 that alert physicians brought to the attention of the C.D.C. a mini-epidemic of immunodeficiency and pneumonia caused by unusual organisms (a fungus called Pneumocystis carinii, and a virus called CMV) in homosexual men in Los Angeles.

Because many of the first people to contract AIDS had had sexual contact with each other, C.D.C. researchers thought they might be looking at an unknown sexually-transmitted infectious disease. They also toyed for a time with the idea that sex-stimulant-chemical use or illicit narcotic use, both very common among the first cases of AIDS, might be somehow causing immunosuppression. Perhaps sexual contact was a red herring--or merely a marker for a small and fairly tight-knit sub-community of people who shared common interests in non- sexual activities which might be damaging their immune systems.

Those physicians treating infectious diseases in homosexual men thought not, however. Dr. Joel Weisman, one of the first doctors to put the AIDS puzzle together, noted that initially, within the male homosexual community, the disease seemed to follow lines of sexual contact more than it did drug or sex habits. Not all homosexual men were so promiscuous as to make contact-tracing impossible; Weisman observed that promiscuous men did not always contract the disease, but on the other hand, that even men with few sexual contacts were coming down with the disease if they had had sexual contact with the wrong person. In fact, men with severe immunodeficiency were eventually found to form sexual contact networks, of the kind that have always been seen by researchers using the classic epidemiologic tools for tracing sexually transmitted disease chains. The difference, however, was that for AIDS the contact networks stretched over years, indicating an infectious agent (if there was one) with a very long latency. Still, investigators found that of the first 19 cases of AIDS reported in Los Angeles, nine had direct or indirect (one intermediate partner) sexual contact with a single French-Canadian airline steward (previously mentioned), a man who was also sick with immunodeficiency.

Then, starting in 1982, reports began to come into the C.D.C. of the same CD4+ lymphocyte and lymphatic-tissue- destroying immune failure syndrome occurring this time in U.S. citizens who had received transfusions. Soon also came reports that an identical immune deficiency of a new severe variety was now being seen in men with hemophilia, a genetic disease in which sufferers must be injected with concentrates of protein clotting factors made from donated blood plasma. Reports of the first people with hemophilia and AIDS emphasized that, in these people, none of the same drug or male-homosexual behavioral factors were present that had been seen in the first group of AIDS sufferers.15

Further, the same was true of those with "transfusion- related AIDS," who also did not fit into drug-using or male- homosexual lifestyles, and did not resemble them in sex or age either. Former tennis star Arthur Ashe is a well-known modern example. Ashe, like many of those with transfusion- related AIDS, had never had an intimate connection with

anyone else with an immune problem, except for a history of blood transfusions years in the past, during the time in which transfusions were associated with AIDS.

In late 1982 all this worried epidemiologists as the reports continued to come in. They knew that another viral disease called hepatitis B ("serum hepatitis") was also transmitted epidemically as a sexually transmitted disease in homosexual men, but much more rarely in homosexual women or heterosexuals in the U.S. Hepatitis B had historically also shown up early in people with hemophilia, who because of their large pooled blood-product exposure have historically seemed to be first to suffer from any new organism infecting the blood supply. Hepatitis B had also been known to be one of the worst disease-causing contaminants in donated blood for general transfusion. Thus, the same three groups of people who had historically been infected with a new epidemic of hepatitis B in the 1970s, had now started coming down with AIDS. Hepatitis B was also a disease of IV drug users who shared needles, and it was not long before the first reports of IV drug users with AIDS came in.

By 1983, the C.D.C. was sure it had a new infectious disease on its hands, similar in epidemiology to hepatitis B but with a longer latency period. Analysis of the habits of donors of the blood components that went into those people who had later developed AIDS, indicated one thing different about the donors: it was found that blood products AIDS patients had received had more often come from people who themselves were at "high-risk" for AIDS due to promiscuous male homosexual behavior. On the other hand, matched case- controls who had been transfused identically from the same blood bank but had not developed AIDS after transfusion, were found to be not nearly as likely to have gotten blood components from anyone in a "high-risk group."

This initial study concluded that there was only a 1% chance that the statistical association of transfusion- associated AIDS with the lifestyle of the blood-donor would be as close as it was found to be, if only chance had determined the lifestyles of the donors of blood to people who later became sick. Such a chance association would have been expected if there was no contamination, and instead there was something about normal transfusion blood itself, or perhaps some other factor unrelated to transfusion, that was causing AIDS in transfusion recipients.16 The remarkable fact--from which there was no escape--was that AIDS in a transfusion recipient predicted the lifestyle of a blood-donor he or she had never met (a donor which generally turned out to be a promiscuous homosexual man who had thought himself to be perfectly healthy). Nothing but an infectious agent could explain a statistical connection between a blood donor's sexual habits, and risk to the person receiving the blood. As for drugs or immune toxins, it was impossible to believe that any chemical toxin could be present in a relatively small amount of blood component coming from a single nominally healthy person, in sufficient quantities to cause total immune failure in the recipient, and do it years after the transfusion.

Eventually, with many cases like Arthur Ashe's on record (but showing up in the early 1980s, earlier than Ashe's did), AIDS looked epidemiologically very much like hepatitis B. The hunt was on for the microbe, or microbes, which caused the new syndrome. When

the virus now known as HIV finally hit the world news in the Spring of 1984, there was a great deal of skepticism in the scientific and lay communities alike. With the ability to test for antibodies to HIV in 1985, however, there came a way of powerfully sifting through putative causal factors for AIDS, and comparing them with the factor of past HIV infection. HIV infection has emerged from these tests as the clear champion of competing AIDS-causation theories, convincing at present all but the most die-hard skeptics.14

Attacks on Straw Men

It is an unfortunate fact that a great deal of the debate over AIDS and HIV has been over what rhetoricians call "straw men." A straw man is an argument or viewpoint set up in a debate only for the purpose of being knocked down, and one which the opposite side never really defended or held; or one which is not very important to the central issue of the debate, even if it has been held. Straw man arguments often result from debaters talking "past each other," without understanding the opposing side's position. In the HIV/AIDS debate, straw men set up by heretics have most often been medical hypotheses which have previously been put forth in the context of the HIV theory and which have turned out to be wrong, but which were never important corollaries necessarily deduced from the idea that HIV causes AIDS. Other straw men are ideas that the orthodox scientific "establishment" never put forth seriously at all, though they may be attacked vigorously by heretics as though they are current medical dogma. We will presently see samples of both.

An example of an epidemiologic straw man is the timing of HIV arrival in the Western hemisphere. Root-Bernstein discusses cases of possible AIDS as far back as 1932, notes documented HIV infection with AIDS as far back as 1968 in the U.S., and argues that these data are anomalous (p. 2) if the virus was transferred for the first time to the Western hemisphere around 1978, as was originally thought. And so they are. But if the HIV virus was transferred much earlier than 1978 to the new world, and remained at low levels in male homosexuals and injecting drug users in America until changing social factors in the 1970s encouraged its spread (exactly as Root-Bernstein himself indirectly suggests), no real damage would be done to a suitably modified HIV/AIDS theory.

An example of a bad prediction made by the orthodox medical establishment which is not necessarily derivative of the HIV theory, was (or is) the official idea that AIDS is due to be a heterosexual pandemic in America any time now. It is argued by Duesberg (p. 203), that the "viral hypothesis" has failed to predict the course of the AIDS epidemic--namely that AIDS has (at least so far) shown no clear inclination to spread rapidly by a complete heterosexual-sexual-transmission mechanism in the U.S., even though it apparently does so in Africa. It is also asserted in a related argument by Root- Bernstein that the HIV/AIDS hypothesis does not explain the generally-low measured levels of HIV virus in semen, the low (but not zero) rate of HIV infection in mates of HIV-positive men with hemophilia, or the nearly zero rate of infection in U.S. heterosexual prostitutes (unless they are drug users). If AIDS is an infectious disease, ask the skeptics, then why does HIV not infect very well?

All these arguments are against straw men. There is nothing in the HIV/AIDS theory which demands that any particular transmission mechanism be the chief cause of the spread of HIV infection in any given place, or which demands that the HIV virus be as infectious in one locality as another. For example, it now seems likely from many studies that sexual transmission of HIV often requires mucosal tissue trauma, which is much more likely with anal intercourse, and/or a concomitant inflammation or ulcer from a second sexually transmitted disease. Because transmission may be inefficient even so, promiscuity also greatly enhances the chance of HIV spread. These requirement(s) for efficient HIV sexual transfer easily explain the difference between spread of HIV in tropical Africa vs. the developed countries. They also adequately explain why a disease which spreads well sexually only in populations with an extreme level of both promiscuity and rectal mucosal trauma (i.e., one sub-segment of American homosexual men) has not yet become a generally spreading sexually-transmitted disease epidemic in the U.S.

It is not that the HIV/AIDS heretics have not come across such explanations. Root-Bernstein, in a good discussion of the epidemiology of AIDS, admits that there is nothing especially strange about a sexually transmitted disease which spreads easily in homosexual males but not heterosexuals in the U.S. Both syphilis and hepatitis B in the 1970s have been examples of such a phenomenon, and the "odd" differential epidemiology of both diseases with regard to sexual- preference groups is easily explained by differential behavior in the homosexual and heterosexual populations in those years.

Duesberg argues that a disease which restricts itself to classes of people in America, but not in Africa, cannot be explained by a micro-organism. But while he is doing so, fellow heretic Root-Bernstein (pp. 281-303) is noting that infectious epidemiology in one group of American homosexual males, who might be sexually infected with giardia, parasites, amoebas, hepatitis A, and B, shigella, salmonella, etc., may resemble far more the disease epidemiology of some African countries than that of heterosexuals living next door (p. 290). In this, an AIDS caused by an infectious agent such as HIV may behave just as AIDS statistics suggest it does, and yet merely follow a pattern already amply demonstrated before AIDS, with many another infectious disease. Root- Bernstein is sometimes too competent a scholar for his own good. His Chapters 8 and 9--which address the epidemiologic differences and commonalities of U.S. homosexual men and African heterosexuals due to sexual practices and social changes which appeared newly in the 1970s and 1980s--not only believably explains and refutes most of Duesberg's epidemiologic problems with AIDS (p. 209), but also does the same with many of Root-Bernstein's own epidemiological problems, raised in Chapter 1.

Unfortunately, Root-Bernstein is willing to let lifestyle and habit differences explain epidemiologic differences when it suits his argument's needs, but much less willing to consider them when they don't. An illustrative example occurs as Root-Bernstein discusses the rectal traumas and infections which occur during certain male homosexual practices, writing of these (p. 283-4): "It is now accepted that such injuries and infections

greatly increase the risk of concurrent infections (HIV or otherwise) and of semen gaining access to the immune system following anal intercourse."

Yet when Root-Bernstein discusses the statistical association of AIDS with receptive anal intercourse (p.225) he shows an odd difficulty with the same concept: "One possibility is that it is much easier to transmit HIV to a receptive partner than from a receptive partner. No other sexually transmitted disease behaves this way, however . . . . HIV would be the first disease agent to be able to make the discrimination, unless some other factor is involved."

Here, unfortunately, Root-Bernstein is wrong, and wrong for the very reasons that he himself discusses in the quote preceding the last. Much like HIV, hepatitis B infection in homosexual men also correlates with rectal trauma and receptive anal intercourse,32 and there is little reason to believe that the "other factor" is anything other than the fairly straightforward mechanical injury that Root-Bernstein has already helpfully identified for us (see reference 33 for statistical development of a "rectal trauma index" which partly predicts risk of HIV infection). It is a characteristic of Root-Bernstein's style of argument that it makes causal mechanisms as mysteriously complicated as possible--very often far more complicated than required to explain the facts.

Root-Bernstein, eager to draw attention to any factor other than HIV in the causation of AIDS, does not take into account the most obvious physical factors: "what is clear from existing studies," he asserts (p. 45), "is that HIV is extremely difficult to transfer to a healthy individual." In fact, existing studies establish no such thing. Studies quoted by Root-Bernstein never demonstrate that only "unhealthy" people in known risk groups contract HIV, only that certain traumatized risk groups (promiscuous gay men, hemophiliacs, transfusion recipients) are on average somewhat unhealthy to begin with. This, of course, is not the same thing. Indeed, there is evidence that within risk groups, even the healthiest of individuals (immunologically) are capable of contracting HIV. Although men with hemophilia and homosexual men are on average mildly immunosuppressed even in the absence of HIV, it is by no means true that all are. A study of army recruits (surely a carefully screened group for health) shows that those who seroconvert to HIV (demonstrating new HIV infection) may initially (by the criterion of CD4+ count) have immunity which is in the normal range. This is true in other groups as well.34

Perhaps the most bloated straw man assailed by Root- Bernstein (and the one that provides the major theme of his book) is the idea that the causal agent of an infectious disease such as AIDS must be both necessary and sufficient to cause the disease in every sense of the terms; and moveover that since Dept. of Health and Human Services Secretary Margaret Heckler's dramatic announcement in 1984, most scientists have considered HIV to play this very role for AIDS. Root-Bernstein spends much time attacking what he calls the "HIV-only" theory of AIDS, an idea which actually has never flown, except possibly in the popular press or the occasional scientist who expresses a rash opinion (Dr. Robert Gallo, official co-discoverer of HIV, must by now badly regret his hyperbole about HIV being able to cause AIDS in Clark Kent35). The subtitle

warning of Root-Bernstein's book is The Tragic Cost of Premature Consensus, and it appears from the book that it is upon the "HIV-only" theory of AIDS that the "premature consensus" of the establishment is in dire danger of settling, if it has not already.

Fortunately, it can safely be said that no such thing is occurring in the biomedical consensus, or about to. This does not prevent Root-Bernstein (p. 331) from logically blasting the somewhat cartoonish view he attributes to medical science: "Two of the most important implications of the HIV- only theory of AIDS are that all the risk groups should develop AIDS at approximately the same rate following HIV infection and that the symptoms they manifest should, on the whole, be the same."

Alas for Root-Bernstein, however, since AIDS has from the beginning involved opportunistic infection organisms which vary in prevalence among populations, and since there has been reason to believe from the first that AIDS risk varies greatly with the biological age of the HIV-infected person, scientists have never, even at the beginning, seriously considered such a theory as Root-Bernstein here lays out: One logical implication is that the immunological status of an infected person should be irrelevant to susceptibility to contagion or to the progression from infection to disease. Acquisition of the retrovirus should be the sole factor determining whether an individual develops AIDS. Everyone should be at equal risk for AIDS, just as everyone is at equal risk for hepatitis B virus, syphilis, or measles.

The most troubling thing about such writing is that an unwary lay reader may leave Root-Bernstein's book with the impression that the author has single-handedly discovered that infectious disease risks depend partly on host immune defenses and host behaviors and environments. The reader might well decide further that the biomedical community today does not in general think in terms of individuals having differing resistances to various diseases, and is accepting such advanced ideas only under duress, due to political pressures resulting from the penetrating logic of popular writers such as Root-Bernstein, who are "re-thinking AIDS."

The facts are more mundane. Obviously, since no microbe infects 100% of people exposed to it, or even causes disease in 100% of the people it infects (not even HIV has been shown to do this), there must be other factors to explain why some exposed people become ill with ANY infectious agent (viral, bacterial or parasitic), and some do not. Medical science certainly recognizes such factors, but does not use them to argue that there is in general something badly wrong with the germ theory of disease. Instead, as discussed earlier, medical scientists regard "causality" in infectious disease in merely the sense of "necessity" (i.e., the "causal" microbe is necessary, but not sufficient). Medicine has not regarded the pathogenesis of any natural infection in terms of a "germ only" theory such as Root-Bernstein describes, since Pasteur, referring to disease, said: "The seed is nothing, and the soil is everything." Thus, Root-Bernstein spends many chapters assailing an idea that physicians have not held since the late 19th century, and certainly have never generally held in the case of AIDS.

No infectious agent is usually "sufficient" to cause disease in a natural host, although in a laboratory (or perhaps very occasionally in nature) it may be sometimes true that the dose may be so high as to make host resistance almost irrelevant. Naturally-occurring infectious disease organisms at reasonable doses, however, always rely on a chink of some kind in host immunity with regard to that particular microbe (this is not to say that we must consider any host that is successfully infected to be "immunocompromised"--that would cheapen and overly broaden this useful term). The idea that deficiencies in host defense in some sense "permit" all or most infections is indeed a standard medical teaching,36 although a lay reader of Root- Bernstein might be surprised to learn of it after Root- Bernstein finishes misrepresenting the standard views of modern medicine.

"Why is there such a huge and medically unprecedented variation in time between HIV infection and death from AIDS?" asks Root-Bernstein (p. 89). The answer to this rhetorical question is that such variation is not medically unprecedented. Other infectious diseases, from malaria to syphilis to tuberculosis to viral hepatitis, may kill years after initial infection--or within a much shorter time. In a cohort of newly-infected people, any study of a chronic infectious disease cannot help but produce steady increases in the "average" time between infection and death, as deaths accumulate slowly while the study follows the infected cohort prospectively onward in time.

"No theory based solely on HIV can explain the phenomenon of variable times of death," writes Root-Bernstein (p. 89). This is correct so far as it goes, but it says much less than it seems to, for this much is true of every infectious disease known, including other infectious diseases which may have latency times to death fully as long as those for HIV. Too much of Root-Bernstein's Rethinking AIDS consists of arguments that the HIV hypothesis needs to be re-thought because HIV infection supposedly has strange properties-- properties which on close examination turn out to be broadly similar to those of many other infectious diseases.

SIDEBAR: What Is a Retrovirus?

A retrovirus is a virus which has its genetic structure encoded into RNA, but which reproduces by turning it back into DNA during an infection. Once inside a living cell, retroviruses are able to synthesize virus DNA-copy molecules using the virus's RNA genetic molecules as a template, or "master" (this process proceeds retrograde to the normal "DNA-->RNA" information flow in cells, hence the name). To do this job a unique enzyme molecule called "reverse transcriptase" is used by the virus. Since this enzyme is not found in normal cells the virus itself must carry it. This enzyme and the process it catalyzes are so unusual in biology that H. Temin and D. Baltimore were awarded the 1975 Nobel Prize in Medicine for discovering it.

Once the DNA-copy of a retrovirus (called a pro-virus) is made, it is often inserted into the DNA of the cell being infected. Now an actual part of the genetic code of the cell, the retrovirus genetic information is hidden from the immune system, which would otherwise destroy the virus inside the cell, or destroy the entire cell. All humans harbor some foreign retroviral DNA actually integrated or inserted into the DNA in most of their body

cells. In this sense, we all share some of the fate of the scientist in the remake of the movie The Fly, a matter-transporter victim whose DNA is not pure and not entirely human, but who cannot do anything about it because there are no "tweezers" fine enough, or discriminating enough, for the job. Some of the foreign DNA in each of our cells is from retroviruses which went into hiding eons ago in our ancestors, and are now reproduced automatically along with our normal cells, and have long since "forgotten" how to get themselves back out of our DNA.

SIDEBAR: What Does "HIV-Positive" Mean?

Antibodies are blood proteins made by immune cells, which stick very specifically to microbial invaders, targeting them for destruction by the immune system. For many years after an infection by a microbe, antibodies specific to that microbe can be detected in the blood. A person who tests positive for antibodies to HIV by two different kinds of lab tests, is said to be "HIV-positive."

In the case of infection with the average microbe, a person may test antibody positive for years or even a lifetime after the microbe is completely gone from the body. For the chronic viruses which hide in cell nuclei, however (retroviruses like HIV; and also CMV, EBV, and other herpes- class viruses), the presence of antibody is generally a clue to the continued presence of the virus, active or inactive, somewhere in the body. In some cases modern sensitive tests for viral DNA can actually detect these hidden viruses directly.

Over the years since the discovery of HIV, critics of the HIV/AIDS hypothesis have had to struggle to keep up with sensitivity increases in HIV testing. Initially, critics complained that HIV virus was not present in most HIV- positive people. When it became clear that infectious virus could be found in almost 100% of such people (if cultures were done correctly) critics claimed that most HIV was dormant until reactivated in culture. With new sensitive tests for HIV RNA showing that HIV virus is active in the body's lymph nodes, critics have fallen back to the position that it may be active, but not active enough. This is a question which can only be answered indirectly, by other studies. Ellison and Duesberg assert (p. 124) that HIV is rarely to be found budding from cells in patients, and that "...in most individuals with AIDS, no virus particles can be found anywhere in the body," implying that this absolves the virus from any disease role. Actually, however, even actively reproducing HIV may spend very little of its total life-cycle budding through a cell membrane or floating free as a particle in the blood before being picked up by another cell. Studies of viral RNA in the body show that there may be anywhere from roughly 10 million, to as much as one billion particles or actively replicating HIV genomes in a gram of lymph tissue--a significant amount by the standards of most other kinds of virus.122

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